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Review article

Dependence of future mortality changes on global CO_2 concentrations: A review

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ABSTRACT

The heterogeneity among previous studies of future mortality projections due to climate change has often hindered comparisons and syntheses of resulting impacts. To address this challenge, the present study introduced a novel method to normalize the results from projection studies according to different baseline and projection periods and climate scenarios, thereby facilitating comparison and synthesis. This study reviewed the 15 previous studies involving projected climate change-related mortality under Representative Concentration Pathways. To synthesize their results, we first reviewed the important study design elements that affected the reported results in previous studies. Then, we normalized the reported results by CO_2 concentration in order to eliminate the effects of the baseline period, projection period, and climate scenario choices. For twenty-five locations worldwide, the normalized percentage changes in temperature-attributable mortality per 100 ppm increase in global CO_2 concentrations ranged between 41.9% and 330%, whereas those of total mortality ranged between 0.3% and 4.8%. The normalization methods presented in this work will guide future studies to provide their results in a normalized format and facilitate research synthesis to reinforce our understanding on the risk of climate change.

1. Introduction

The effects of temperature elevations due to climate change on future mortality have been well studied. Elevated temperatures directly increase thermal stress leading to increased number of heat cramps, heat syncope, heat exhaustion and heat stroke (Patz et al., 2000) as well as cardiorespiratory mortality (Liu et al., 2011). Gasparrini et al. (2015) collected historical data from 384 locations in 13 countries worldwide and showed that the heat-related all-cause (or non-external-cause where not available) mortality increases with temperature in all studied countries. Liu et al. (2011) demonstrated a causal link between the elevated temperature and increased cardiorespiratory mortality in Beijing, China. In addition, shifts in global temperatures are expected to cause the increased intensity and frequency of extreme weather events such as heat waves, floods, storms, and droughts (Forzieri et al., 2017; Lee and Kim, 2017), as well as proliferation of microbial food poisoning and vector-borne infectious diseases (Patz et al., 2000; McMichael et al., 2006).

The Fifth Assessment Report of the Intergovernmental Panel on Climate Change (IPCC) concluded that without a successful mitigation of greenhouse gas emissions, the global mean temperature would increase by $> 2\,^{\circ}C$ by the end of the 21st century, eventually leading to increases in heat-related mortality (IPCC, 2014). Given the importance of elevated temperature with regard to future human health, many studies initially investigated the associations between temperature and mortality and subsequently attempted to project temperature-related mortality using future temperature profiles obtained from various global circulation models (GCMs) under benchmark climate scenarios such as Representative Concentration Pathways (RCPs).

Although several review studies have attempted to synthesize these previous projection studies (Huang et al., 2011; Hajat and Kosatky, 2010; Boeckmann and Rohn, 2014; Sarofim et al., 2016), to our knowledge, none has successfully achieved a quantitative synthesis or comparison of the magnitudes of future health impacts. We attribute this lack of success to the high levels of heterogeneity among previous studies with respect to the study location and period, climate models, statistical methods, and even the presentation of results. Accordingly, it has not been possible to integrate these studies and reach a comprehensive understanding of the temperature-related mortality risks attributable to climate change. Furthermore, this heterogeneity has increased the difficulty of research synthesis, as the different study designs have influenced the various results. Previous review studies

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have therefore provided only compilations and categorizations of projected future health effects (Huang et al., 2011; Hajat and Kosatky, 2010; Boeckmann and Rohn, 2014).

As we believe that it is necessary to integrate the projected results if we are to understand the global impacts of climate change on human health, the present study comprises a systematic review of 15 previous studies that projected future temperature-related mortality under RCP scenarios and summarization of the respective methods and major findings. Our method summarization process involved a careful selection of the important study design elements, such as study targets and statistical methods that would have affected the reported results, as well as the popular choices for the elements in previous studies, to provide an insight into the widely accepted methods for projection study design. Next, we normalized the reported mortalities from each study with respect to changes in global CO_2 concentrations to provide the first comparison of the magnitude of health effects. Our normalization methods allow a comparison of these various projection results, as well as a research synthesis to obtain a more comprehensive understanding of the mortality risks due to climate change. This study is important because it is the first to review RCP scenario-based projection studies, and because it is also the first to devise a novel normalization method and provide a guide towards research synthesis.

2. Methods

2.1. Search strategy and selection criteria

The Google Scholar, Science Direct, PubMed, Scopus, and Web of Science search engines were used from January 1st to February 28th, 2017 to identify published research articles written in English in the scope of epidemiological research. The following keywords were used in this literature search: projection, mortality, climate change, RCP, temperature, heat, and health effect. Three major criteria were used to select published studies for inclusion in this review article. First, the articles were required to project future temperature-related mortality based on at least one RCP scenario. Second, the association between temperature and temperature-related mortality had to be obtained using historical data. Lastly, only peer-reviewed studies were considered; books, reports, and abstracts were excluded.

2.2. Research synthesis strategy

The heterogeneity among previous studies of mortality projection presents a particular challenge to synthesis. Therefore, we first carefully listed and summarized the 21 study design elements that affected the reported results in each previous study. Next, we used normalization to eliminate the effects of the baseline period, projection period, and climate scenario choices (see the following subsections for more details). To eliminate the confounding contributions of exposure variable (temperature or heat wave), adaptation and population change, we only synthesized the previous projection results that were based on temperature exposure with an assumption of no adaptation and constant population.

2.3. Conversion of compiled results into relative risks

Previous studies reported their projection results in various formats such as relative risks (RRs), percentage changes, additional mortality rates or counts, projected mortality rates or counts, and/or projected attributable fractions. As the first step towards our research synthesis, we converted all compiled results to relative risks, which were defined as shown below.

$$\mathrm{RR} = \frac{\text{projected annual mortality count}}{\text{baseline annual mortality count}} \quad (1)$$

These conversions were performed using the equations given in Supplementary Section 1. We obtained all information needed for conversion from the previous study reports and supplementary materials. Reports that did not provide sufficient information for conversion were excluded from the research synthesis.

2.4. Normalization of relative risks based on global CO_2 concentrations

The conversion to RR for each projection study did not provide a sufficient basis for comparison because the baseline period, projection period, and climate scenarios, all of which affect the RR values, differed among studies. In this study, we applied a novel normalization method for reported or converted RR values based on the historical and projected global CO_2 concentrations. First, we obtained the average annual global CO_2 concentration levels during the baseline and projection periods under the given climate scenario. Next, we calculated the increase in the average global CO_2 concentration level (ΔCO_2) from the baseline to the projection period. Finally, we performed a linear regression between the converted relative risks and the ΔCO_2 to yield a normalized percentage change (NPC) in mortality per 100 ppm increase in global CO_2 concentration. Additionally, we checked the scatter plots to justify the use of a linear regression.

3. Results

Using our search criteria, we identified 15 studies that had projected future temperature-related mortality under RCP scenarios (Petkova et al., 2017; Gosling et al., 2016; Kim et al., 2016; Kingsley et al., 2016; Lee and Kim, 2016; Li et al., 2016; Marsha et al., 2016; Martinez et al., 2016; Li et al., 2015; Murari et al., 2015; Schwartz et al., 2015; Kim et al., 2014; Stone et al., 2014; Wu et al., 2014; Petkova et al., 2013). We found two additional studies (Hsiang et al., 2017; Gasparrini et al., 2017), which were published after writing this review. These two studies were referenced but not included in the review. The first of these studies was published in 2013, and we observed a rapid increase in the number of published studies since that year. All 15 studies used roughly the same process to project future mortality due to climate change, which comprised an initial model of the exposure-response relationship, projection of the level of future exposure based on GCMs under RCP scenarios, and an estimation of future mortality. However, the details of these studies varied widely in various aspects, including the target of interest, analytical methods, and results presentation.

As a careful understanding of the design selections made by previous studies is important for a research synthesis, we thoroughly and carefully selected 21 study design elements that would be expected to have influenced the projection results. Table 1 lists these elements, as well as the previous studies that selected each, based on popularity. The count numbers for each choice among the previous studies are listed in parentheses. In the following sub-sections, we have analyzed each of three categories in study design elements in greater detail.

3.1. Study target

For the study target category, we selected six elements for summary (see Table 1). Supplementary Table S1 additionally summarizes the study target for each of the 15 projection studies in reverse chronological and alphabetical order. The previous studies were conducted in various locations, including seven in the Americas (all in USA), six in Asia (two in China, one in India, and three in South Korea), and two in Europe, and were based on diverse modeling, baseline, and projection periods. The modeling period indicated the period during which historical time-series data were used to extract the exposure-response relationship, whereas the baseline and projection periods indicated the periods during which the baseline and projected mortalities were calculated, respectively. These study periods have significant influences on the results and are therefore considered very important projection parameters.

Table 1
Categories and statistics.

Category	Study design element	Choice (count)
Study target	Location	1. America (7) 2. Asia (6) 3. Europe (2)
	Study period	Summarized separately in Supplementary Table S1
	Season	1. Warm season (10) 2. All seasons (5)
	Exposure of interest	1. Temperature (12) 2. Heat wave (3)
	Exposure category	1. Heat (13) 2. Heat and cold (2)
	Response of interest	1. Non-accidental mortality (9) 2. All-cause mortality (4) 3. Multiple-cause mortality (2) 3. Cardiovascular mortality (2) 4. Respiratory mortality (1) 5. Heat-related external mortality (1)
Exposure-response relationship modeling	Statistical category	1. Regression (14) 2. Substitution (1)
	Statistical method	1. GLM (11) 2. DLNM (4) 3. GAM (1)
	Distribution	1. Poisson (5) 2. Quasi-Poisson (4) 3. Gaussian (2) 4. Negative-binomial (1)
	Model	1. Linear threshold or linear (11) 2. Natural cubic spline (3) 3. Quadratic spline (2) 4. Quadratic (1)
	Lag structure	1. None (8) 2. Single lag (5) 3. Basis (4) 4. Multiple lag (1)
Future exposure and response predictions	Climate model	Summarized separately in Supplementary Table S3
	Climate scenario	1. RCP 8.5 (13) 2. RCP 4.5 (12) 3. RCP 2.6 (3) 4. RCP 6.0 (2)
	Adaptation	1. No (12) 2. Yes (3)
	Adaptation method	Summarized separately in Supplementary Table S3
	Population change	1. None (6) 2. Total population change only (5) 3. Both total and compositional changes (3) 4. Compositional change only (1)
	Socioeconomic change	1. No (14) 2. Yes (1)
	Population/ socioeconomic change method	1. Cohort component (7) 2. Generalized cohort component (1) 3. Extrapolation (1)
	Population scenario	1. Business as usual (4) 2. Single component variants (4) 3. SSP (1) 4. Exponential or logistic (1)
	Socioeconomic scenario	1. SSP (1)
	Population group	1. All (11) 2. Age groups (3) 3. Socioeconomic groups (1)

Regarding the exposure of interest, 12 studies used temperature as the exposure variable, with mortality modeled as a function of temperature (Petkova et al., 2017; Gosling et al., 2016; Kingsley et al., 2016; Lee and Kim, 2016; Li et al., 2016; Marsha et al., 2016; Martinez et al., 2016; Li et al., 2015; Schwartz et al., 2015; Kim et al., 2014; Stone et al., 2014; Petkova et al., 2013), whereas three studies used the intensity or frequency of heat wave as the exposure variable (Kim et al., 2016; Murari et al., 2015; Wu et al., 2014). Most studies focused only on heat-related mortality (Petkova et al., 2017; Gosling et al., 2016; Kim et al., 2016; Kingsley et al., 2016; Li et al., 2016; Marsha et al., 2016; Martinez et al., 2016; Li et al., 2015; Murari et al., 2015; Kim et al., 2014; Stone et al., 2014; Wu et al., 2014; Petkova et al., 2013), although two investigated both heat- and cold-related mortalities (Lee and Kim, 2016; Schwartz et al., 2015). As most of the previous studies focused on the heat effects of temperature, they typically chose to focus on warm seasons. Regarding the response of interest, non-accidental mortality was the most popular choice, followed by all-cause mortality.

3.2. Exposure-response relationship modeling

For exposure-response relationship modeling, we selected five elements for summarization (see Table 1). Supplementary Table S2 summarizes these elements for the 15 included projection studies. When modeling their exposure-response relationships, 14 previous studies used regression methods, whereas one study by Wu et al. simply divided the average mortality rate on a heat wave day by the mortality rate on a normal day to calculate the RR (Wu et al., 2014). For regression-based studies, the generalized linear model (GLM) was the most frequently applied time-series analysis method, followed by the distributed lag nonlinear model (DLNM) and generalized additive model (GAM). The DLNM was recently developed to model complex nonlinear and lagged dependencies between exposure and response (Gasparrini et al., 2010), and the GAM is an extension of GLM wherein degrees of smoothing functions can be determined using a penalized regression method.

Previous studies have assumed either Poisson, quasi-Poisson, negative-binomial, or Gaussian distributions when applying regression methods. The first three assumptions are popular because their natures render them suitable for modeling count data. In addition, the quasi-Poisson and negative-binomial regressions are used for over-dispersed count data. Despite its relative unpopularity, Murari et al. (2015) and Kim et al. (2016) used a Gaussian, rather than a Poisson, regression to model the relationship between heat wave and mortality.

Along with choices in the statistical method and distribution, previous studies also used curves to model the exposure-response relationship. Linear thresholds and linear models are the most popular choices, as these are widely considered to be easily applied and effective for temperature-mortality relationship modeling. The natural cubic spline and quadratic spline were also popular choices for more accurate modeling. Finally, nearly half of the included studies did not model a lag effect, whereas the other half modeled the lag effect using either a basis-based method supported in the DLNM framework or a single lagged variable (either a mere lag or the moving average of a few exposure days). Only one previous study (Stone et al., 2014) used multiple lagged variables to model lagged dependencies.

3.3. Future exposure and response predictions

For the future exposure and response prediction, we selected 10 elements for summarization (see Table 1). Supplementary Table S3 summarizes those elements for the 15 included projection studies. To predict future exposure, the 15 RCP scenario-based projection studies used global circulation models (GCMs) under climate scenarios. The number of different GCMs per study varied from 1 to 42, and RCP 8.5 was most frequently used, followed by RCP 4.5.

The future exposure-response relationship and population must be determined to estimate future mortality under the predicted exposure. The simplest, and therefore most popular, approach involves the assumption that both future parameters are identical to those obtained from historical data (Kingsley et al., 2016; Li et al., 2015; Murari et al., 2015; Schwartz et al., 2015; Petkova et al., 2013). Among the 15 previous studies, only three applied adaptation, whereas eight applied a total population change, four applied a demographic composition change (e.g., age structure or sex composition), and one applied a population socioeconomic change (e.g., educational attainment and

income class). Most previous studies did not assume any adaptation and applied a baseline exposure-response relationship, largely because the rate and extent of the adaptation were unknown; therefore, there is no standard or widely applied adaptation method or scenario (WHO, 2014). Accordingly, the previous studies applied their own adaptation methods. According to Gosling et al. (2016), adaptation methods can be classified into six categories: absolute threshold shift, relative threshold shift, reduction in slope of the exposure response function (ERF), combined absolute threshold shift with reduction in slope of the ERF, combined relative threshold shift with reduction in slope of the ERF, and analogue ERF. Gosling and colleagues demonstrated the potential effects of each adaptation modeling method on future mortality and recommended two adaptation methods, absolute threshold shift and reduction in slope of the ERF, for further projection studies (Gosling et al., 2016). Among the three studies that applied adaption, the most popular methods were slope reduction and a combination of threshold shift and slope reduction. Petkova et al. (2017) assumed a gradual reduction in the slope of the baseline exposure-response relationship during 2000s by 20%, and a reduction of 80% until 2100. Li et al. (2016) assumed 5%, 15%, 30% and 50% reductions in the heat effect using a combined effect of the slope reduction and minimum mortality temperature shift.

To predict future populations, most previous studies used the standard cohort-component method wherein the components of population change, namely fertility, mortality and migration, are projected separately based on population change scenarios (Petkova et al., 2017; Kim et al., 2016; Lee and Kim, 2016; Li et al., 2016; Kim et al., 2014; Stone et al., 2014; Wu et al., 2014). The most frequently used scenario is the so-called business as usual (BAU), which assumes that the fertility, mortality and migration rate will remain constant with the historical level throughout the projection period (Petkova et al., 2017). Otherwise, single component variants are often used to allow a comparison of results when a certain component (e.g., low mortality) is changed. Petkova et al. (2017) used BAU, low mortality, high in-migration, and high out-migration scenarios to consider population change. Lee and Kim divided their total population into four age groups and considered both population and demographic component changes under low, medium, and high fertility scenarios, and observed increased future temperature-related mortality relative to a model that did not include societal aging (Lee and Kim, 2016). In a 2016 study, Li et al. targeted only the elderly group (aged $\geq$65 years) in a study of low, medium, and high fertility scenarios (Li et al., 2016).

In addition to conventional population predictions, Marsha et al. (2016) also considered socioeconomic change in prediction when defining four vulnerable groups, namely the elderly (aged 66 and more), infants (aged 0–4), those living alone, and those living in poverty, and estimated the future populations of these groups separately under two Shared Socioeconomic Pathway (SSP) scenarios (SSP3 and SSP5) (Marsha et al., 2016). SSPs comprise a group of scenarios recently developed to serve as a basis for socioeconomic prediction (O'Neill et al., 2014). These scenarios can be used with a generalized extension of the standard cohort-component method, wherein the population is divided into sub-groups not only by age, sex, and region, but also by socioeconomic categories such as educational attainment or income class. Accordingly, group-specific fertility, mortality, and migration, as well as the inter-group transition rates, become the assumed components for prediction. The assumptions for these components are bundled in each of the SSP scenarios. Finally, the extrapolation method can also be used for population prediction. Martinez et al. used population data from 2002 and 2012 to predict the future population until 2100 based on exponential and logistic models (Martinez et al., 2016).

3.4. Projection results and research synthesis

The major findings and claims of the 15 previous studies are summarized in Supplementary Table S4. The projection results from the previous studies cannot be directly compared because of inter-study heterogeneity. We have listed the 21 heterogeneous factors that might have influenced the projection results in Table 1. To reach a more comprehensive understanding of the impact of climate change based on the previous studies' findings, we subjected the projection results to a format conversion and normalization. First, as shown in Supplementary Table S4, the previous studies reported their projection results in various formats, including projected mortality counts and percentage changes. We converted these results to RR values using the method and equations described in the Methods section. Supplementary Table S4 also summarized the conversion equation applied to each study. All of the converted RR values for the previous projection studies are shown in Supplementary Fig. S1, which depicts the RR trends for each location. However, we could not suitably conduct a quantitative comparison of the results between locations because of the diversity in climate scenarios, baseline periods, and projection periods. Supplementary Fig. S2 provides a graphic depiction of the diverse baseline and projection periods of the included projection studies.

To overcome this problem, we investigated the increase in RR based on the difference between the average global CO_2 concentration levels during the projection and baseline periods under the given climate scenarios for each study. Supplementary Fig. S3 depicts the global CO_2 concentration levels under each climate scenario, and Fig. 1 presents the converted RR values vs. the increase in global CO_2 concentrations. Interestingly, the converted RR values increased linearly with the increase in global CO_2 concentrations (the fitted black lines indicate the results of each linear regression). The R-squared values of the linear regressions were summarized in Supplementary Table S5. Finally, we normalized the converted RR values to the percentage changes per 100 ppm increase in CO_2 levels using the slope obtained from the linear regression analysis (see the Method section for more details).

The normalized percentage changes (NPCs) per 100 ppm increase in CO_2 concentration for each study were then summarized to understand the changes in mortality attributable to future CO_2 concentrations (see Fig. 2), and the total and temperature-attributable deaths were plotted separately based on the results of previous studies. As shown, the NPCs in temperature-attributable deaths ranged between 41.9% (New York in Petkova et al. (2017)) and 330% (Philadelphia in Stone et al. (2014)), whereas those of total deaths ranged between 0.3% (Rhode Island in Kingsley et al. (2016)) and 4.8% (Rome in Gosling et al. (2016)). Note that we reported both the NPCs of temperature-attributable and total deaths for Skopje (42.6% vs. 1.4%) because Martinez et al. reported the attributable fractions (AFs) during the baseline and projection periods (Martinez et al., 2016).

4. Discussion

4.1. Pros and cons of normalization based on global CO_2 concentration

The present study normalized the published percentage changes in human mortality with respect to a 100 ppm increase in global CO_2 concentrations. This normalization was used to synthesize the previous projection results with various climate scenarios, baseline periods, and projection periods. For achieving the aim, there are other possible normalization options. One alternative is normalizing to regional temperature increase. In this section, we discussed the pros and cons of each normalization option.

Increase in global CO_2 concentration leads to increase in temperature. This warming is not uniform across the globe but has variation at regional scale. In particular, the temperature increases will be greater over land than oceans or coastal regions and greater at higher latitude regions than the tropics (McMichael et al., 2006). It also depends on the regional land use. For example, urban areas experience heat island effect and warm more quickly than rural areas (Patz et al., 2005). In addition to the regional variations in temperature increase, temperature vulnerability varies from region to region. The slope of temperature-

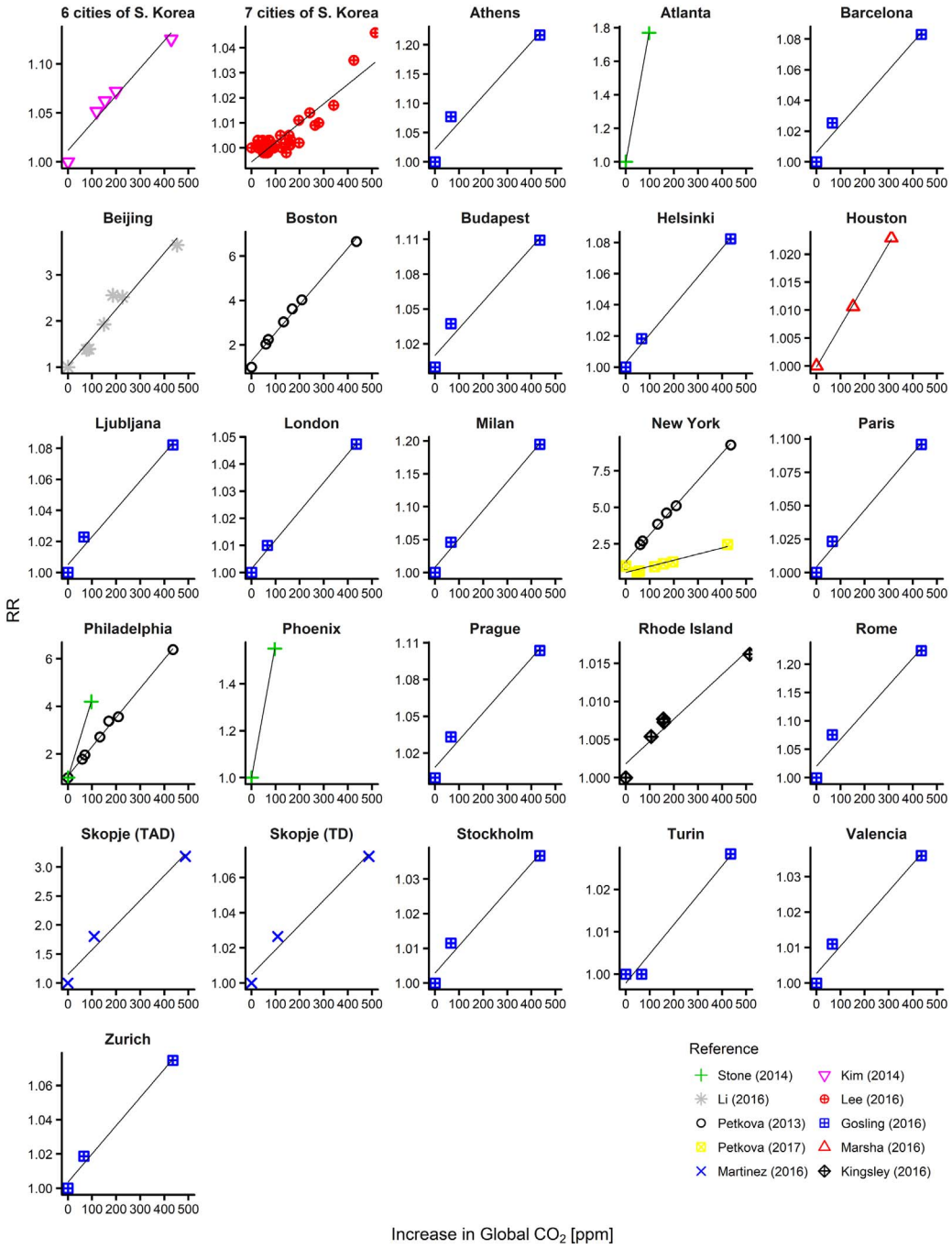

Fig. 1. Relative risks (RRs) of mortality for various baseline and projection periods and climate scenarios, plotted against the increases in global CO_2 concentrations at each location. The lines indicate the linear regression results. In addition to heat wave exposure studies, Schwartz et al. (2015) were excluded because it did not provide sufficient information for conversion to RR. Note that Skopje (TAD) indicates the RR of temperature-attributable deaths (TADs), whereas Skopje (TD) indicates the RR of total deaths (TDs).

mortality relationship is not identical (Gasparrini et al., 2015), nor is the risk of temperature-induced infectious diseases (Patz et al., 2005).

Normalizing to the regional temperature allows for comparing the risk due to equal temperature increase. Such comparison shows which part of the world is more vulnerable to temperature increase than others. On the other hand, normalizing to the concentration allows for comparing the risk due to equal global CO_2 increase. One merit of this normalization is that the additional information required for the normalization is only the historical and projected annual global CO_2 concentration level, which is easy to obtain (see Supplementary Fig. S3), whereas the amount of regional temperature increase is necessary for normalizing with respect to temperature change. Therefore, normalizing to the concentration simplifies the process of synthesizing previous studies where the spatially allocated temperature changes are not accessible. In addition, the temperature-attributable risk per 100 ppm increase in CO_2 concentration is by definition useful information in setting a carbon budget, which is a CO_2 emission budget necessary to keep climate change "tolerable."

4.2. *Effects of confounding variables*

The NPC of New York was obtained to be 185.3% from Petkova's study in 2013 but 41.9% from their other study in 2017. Although those two studies shared many design choices, they incorporated different modeling periods (1985–2006 vs. 2000–2006), seasons (May–Sep vs. Jun–Sep), responses of interest (all-cause mortality vs. multiple-cause

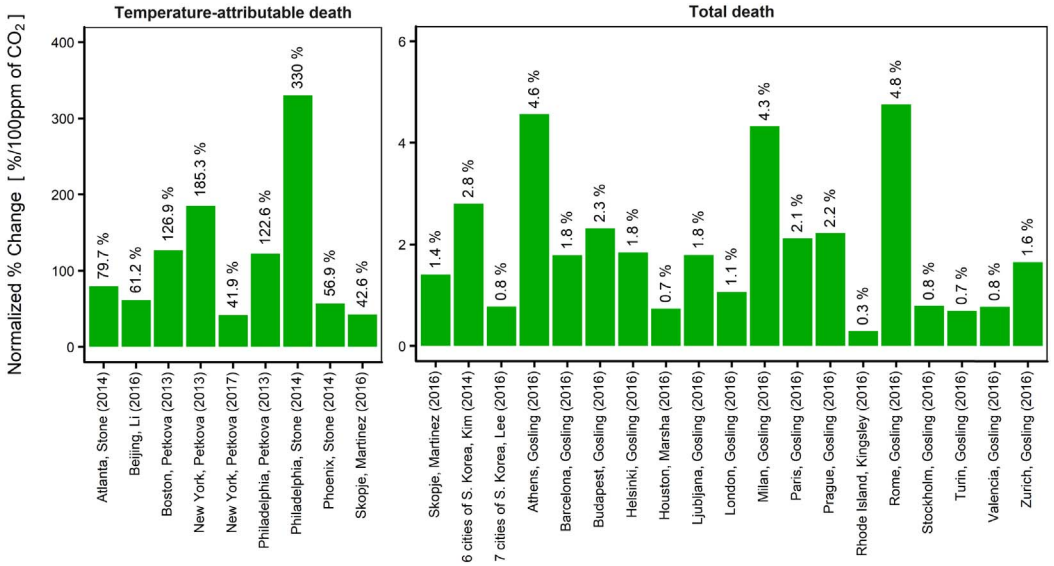

Fig. 2. The normalized percentage changes per 100 ppm increase in global carbon dioxide levels for each location and reference.

mortality), and models (natural cubic vs. quadratic splines). Of these parameters, the modeling period was likely the most important factor affecting the NPC, as the New York population has experienced a rapid heat adaptation since the 1970s due to the widespread use of air conditioning systems (Petkova et al., 2017).

As shown in the above example, confounding variables affected the NPC results. All the study design elements listed in Table 1 and Supplementary Tables S1–S3 can affect the NPC results except baseline period, projection period, climate scenario, adaptation-related variables, and population-change-related variables. Quantifying the effect of the various confounding variables is difficult, and none of the review studies has succeeded in this task to our knowledge. One of the reasons is simply that there is not enough data to rigorously analyze the effects. Therefore, the discussion on the effects of confounding variables presented here is qualitative than quantitative.

For continuous confounding variables (latitude, longitude, number of studied months in a year, and average year of modeling period), we analyzed the scatter plots to examine the relationships between these factors and the NPCs (see Fig. 3). Of these, latitude and longitude did not exhibit the relationship with the NPC, while the other two showed negative relationship. The negative relationship with the number of studied months in a year can be attributed to the decreasing net effect of excess heat by including more months outside the Northern hemisphere summer months, while that with the modeling period can be attributed to the increasing human adaptation observed in later modeling periods, which led to smaller NPCs.

The regional temperature uncertainty predicted by global circulation models (GCMs) is another source of variation in NPCs. GCMs have been developed and improved for a few decades. Today's GCMs include detailed representation of the ocean, land surface, sea ice, and atmosphere, and they have been well validated against the historical data (McMichael et al., 2006). However, there are still residual uncertainties, and the regional temperature predicted by multiple GCMs has variations (McMichael et al., 2006; Benmarhnia et al., 2014; Gosling et al., 2016). As a result, a number of previous studies used an ensemble of GCMs to predict the regional temperature. Nine out of 15 previous studies we reviewed used multiple GCMs to understand the magnitude of variations in predicted temperature and to account for the confounding effects of GCMs. For projection studies, it is highly encouraged to use an ensemble of GCMs and report the variation that stems from uncertainties in GCMs, so that the review studies can compile the ranged risks and used them to synthesize previous studies more rigorously.

In addition, consideration of cold-related mortality is also a confounding factor in calculating NPCs. Among 15 previous studies, 13 studies focused only on heat-related mortality, while only 2 studied both heat- and cold-related mortalities. The implication of including the cold-related mortality is somewhat controversial. A group of studies stated that the increasing temperature is expected to decrease cold-related mortality in future (Li et al., 2013; Doyon et al., 2008; Huang et al., 2012; Hayashi et al., 2012; Martin et al., 2012). However, Patz et al. (2000) argued that the relationship between weather and mortality in winter is still poorly understood, and the net effect of climate change on winter mortality is unknown. Regardless of the controversy, we recommend that projection studies include the impact of climate change on both heat- and cold-related mortalities separately, so that we can understand their risks separately and stratify them to control the confounding effects.

Lastly, mortality type and variables related to statistical methods are also confounders of NPCs. Previous studies analyzed the risks of various types of mortalities, such as all-cause, non-accidental, multiple-cause, cardiovascular, and respiratory mortalities. However, the effects of increased temperature on various mortality types are still unclear. According to Kim et al. (2014), no single type of mortality among all-cause, cardiovascular, and respiratory mortalities is more affected by increased temperature, and rather, the effects are highly location- and age-group-specific. It is also unclear how the use of a certain statistical method or a certain lag structure affects a projection result. One thing that has been known is that the projection will be more accurate with the use of advanced statistical methods such as DLNM (Gasparrini et al., 2010). As a result, further studies are necessary to strengthen our understanding on these confounders.

4.3. Requirements of synthesizable research

Although there are a large number of previous projections studies, we are still far from understanding the true risk of climate change. Researchers have been reporting a wide range of relative risks due to climate change, but due to the high levels of heterogeneity among previous studies, we cannot compare them and understand why the risks are different from region to region. Now, it is time for the community to think about a way to produce work that is more easily compared and synthesized.

Here are some of the requirements to synthesize research by incorporating the methods developed in this work. First of all, future studies should report their results normalized per 100 ppm increase in

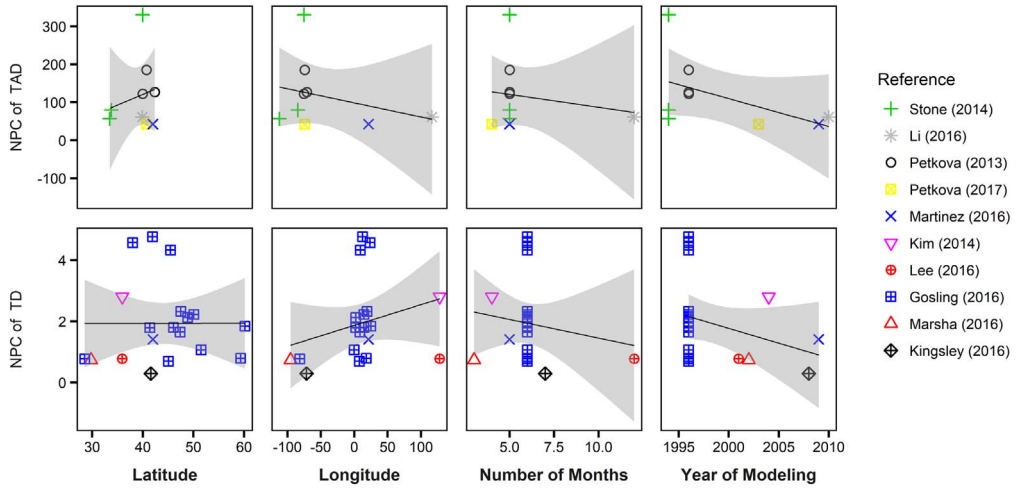

Fig. 3. Normalized percentage changes (NPCs) in temperature-attributable and total deaths against 4 continuous factors: latitude, longitude, number of months studied in a year, and average year of the modeling period.

global CO_2 concentration and also per 1 °C increase in regional temperature, so that readers can easily compare. Second, researchers should provide both the relative risks of temperature-attributable mortality and total mortality or at least provide attributable fraction during baseline and projection periods, so that readers can convert one from another. Third, researchers should provide the result of various sensitivity analysis, including but not limited to the choice of climate models. Lastly, researchers should provide the general information about the studied location such as meteorological, demographic, economical information.

4.4. Future works

This study reviewed the mortality risk attributable to increased temperature and heat waves. However, there are very diverse other pathways by which climate change affects human health (Patz et al., 2000; McMichael et al., 2006). Such pathways include increased intensity and frequency of other extreme weather events such as floods, storms, and droughts (Forzieri et al., 2017; Lee and Kim, 2017), proliferation of microbial and vector species leading to increased risks of food poisoning and infectious diseases, and environmental degradations of crops, livestock and fisheries (McMichael et al., 2006; Hsiang et al., 2017). There are also climate-change-induced air-pollution related mortalities (Patz et al., 2000). For example, elevated temperature increases photochemical reactions to form near-surface ozone, thereby affecting human health (Lee et al., 2017). Lastly, climate change can disrupt the social, economic, demographic, behavioral aspects of human lives (Hsiang et al., 2017). Further studies are needed in the area regarding these other pathways.

In addition, several types of future studies in the area of temperature-attributable mortality risk estimation due to climate change are needed. First, meta-analyses should include in-depth analyses of the contributions of various confounding factors. Second, an understanding of the rate and extent of adaptation and definitions of the standard research methods and scenarios are needed to address the current lack of these options for acclimatization studies. Third, studies of the effects of population and socioeconomic changes on future mortality would provide important and interesting data. Currently, our understanding of how the selection of cohort groups within a population affects the prediction results is lacking, and accordingly it is difficult to synthesize previous studies with different sets of cohort groups.

5. Conclusions

This study reviewed 15 previous studies of future mortality projections under RCP scenarios, with the aim of overcoming the inter-study heterogeneity that has led previous review studies to merely compile and summarize, rather than synthesize the literature. Accordingly, we devised a novel method to normalize the baseline periods, projection periods, and climate scenarios of these 15 studies based on the global CO_2 levels, and reported our comparison of the normalized results for each location and reference. 25 locations worldwide showed very diverse normalized percentage changes (NPCs) in mortality. The NPCs in temperature-attributable mortality ranged between 41.9% and 330%, whereas those of total mortality ranged between 0.3% and 4.8%. We hope that our study will influence future studies to report their results in synthesizable format such as normalized percentage changes and will guide future work that will reinforce our understanding of the risks of climate change.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envint.2018.02.024.

References

Benmarhnia, T., Sottile, M.F., Plante, C., Brand, A., Casati, B., Fournier, M., Smargiassi, A., 2014. Variability in temperature-related mortality projections under climate change. Environ. Health Perspect. 122, 1293–1298.
Boeckmann, M., Rohn, I., 2014. Is planned adaptation to heat reducing heat-related mortality and illness? A systematic review. BMC Public Health 14, 1112.
Doyon, B., Bélanger, D., Gosselin, P., 2008. The potential impact of climate change on annual and seasonal mortality for three cities in Québec, Canada. Int. J. Health Geogr. 7, 23.
Forzieri, G., Cescatti, A., e Silva, F.B., Feyen, L., 2017. Increasing risk over time of weather-related hazards to the European population: a data-driven prognostic study. Lancet Planet Health 1, e200–208.
Gasparrini, A., Armstrong, B., Kenward, M.G., 2010. Distributed lag non-linear models. Stat. Med. 29, 2224–2234.
Gasparrini, A., et al., 2015. Mortality risk attributable to high and low ambient temperature: a multicountry observational study. Lancet 386 (9991), 25–31.
Gasparrini, A., et al., 2017. Projections of temperature-related excess mortality under climate change scenarios. Lancet Planet Health 1, e360–367.
Gosling, S.N., Hondula, D.M., Bunker, A., Ibarreta, D., Liu, J., Zhang, X., Sauerborn, R.,

2016. Adaptation to climate change: a comparative analysis of modelling methods for heat-related mortality. Environ. Health Perspect Available at: http://eprints.nottingham.ac.uk/38535/1/Gosling_etal_EHP_AAM.pdf (in press).
Hajat, S., Kosatky, T., 2010. Heat-related mortality: a review and exploration of heterogeneity. J. Epidemiol. Community Health 64, 753–760.
Hayashi, A., Akimoto, K., Sano, F., Mori, S., Tomoda, T., 2012. Evaluation of global warming impacts for different levels of stabilization as a step toward determination of the long-term stabilization target. Clim. Chang. 98, 87–112.
Hsiang, S., Kopp, R., Jina, A., Rising, J., Delgado, M., Mohan, S., Rasmussen, D.J., Muir-Wood, R., Wilson, P., Oppenheimer, M., Larsen, K., Houser, T., 2017. Estimating economic damage from climate change in the United States. Science 356 (6345), 1362–1369.
Huang, C., Barnett, A.G., Wang, X., Vaneckova, P., FitzGerald, G., Tong, S., 2011. Projected future heat-related mortality under climate change scenarios: a systematic review. Environ. Health Perspect. 119, 1681–1690.
Huang, C., Barnett, A.G., Wang, X., Tong, S., 2012. The impact of temperature on years of life lost in Brisbane, Australia. Nat. Clim. Chang. 2, 265–270.
IPCC, 2014. Climate Change 2014: Impact, Adaptation, and Vulnerability. Part A: Global and Sectoral Aspects. Contribution of Working Group II to the Fifth Assessment Report of the Intergovernmental Panel on Climate Change. Cambridge University Press, Cambridge, United Kingdom and New York, NY, USA.
Kim, Y.–M., Kim, S., Liu, Y., 2014. The impact of climate change on heat-related mortality in six major cities, South Korea, under representative concentration pathways (RCPs). Front. Environ. Sci. 2, 1–11.
Kim, D.–W., Deo, R.C., Chung, J.–H., Lee, J.–S., 2016. Projection of heat wave mortality related to climate change in Korea. Nat. Hazards 80, 623–637.
Kingsley, S.L., Eliot, M.N., Gold, J., Vanderslice, R.R., Wellenius, G.A., 2016. Current and projected heat-related morbidity and mortality in Rhode Island. Environ. Health Perspect. 124 (4), 460–467.
Lee, J.Y., Kim, H., 2016. Projection of future temperature-related mortality due to climate and demographic changes. Environ. Int. 94, 489–494.
Lee, J.Y., Kim, H., 2017. Comprehensive assessment of climate change risks. Lancet Planet Health 1, e166–167.
Lee, J.Y., Lee, S.H., Hong, S.-C., Kim, H., 2017. Projecting future summer mortality due to ambient ozone concentration and temperature changes. Atmos. Environ. 156, 88–94.
Li, T., Horton, R.M., Kinney, P.L., 2013. Projections of seasonal patterns in temperature-related deaths for Manhattan, New York. Nat. Clim. Chang. 3, 717–721.
Li, T., Ban, J., Horton, R.M., Bader, D.A., Huang, G., Sun, Q., Kinney, P.L., 2015. Heat-related mortality projections for cardiovascular and respiratory disease under the changing climate in Beijing, China. Sci. Rep. 5, 11441. http://dx.doi.org/10.1038/srep11441.
Li, T., Horton, R.M., Bader, D.A., Zhou, M., Liang, X., Ban, J., Sun, Q., Kinney, P.L., 2016. Aging will amplify the heat-related mortality risk under a changing climate: projection for the elderly in Beijing, China. Sci. Rep. 6, 28161. http://dx.doi.org/10.1038/srep28161.
Liu, L.Q., et al., 2011. Associations between air temperature and cardio-respiratory mortality in the urban area of Beijing, China: a time-series analysis. Environ. Health 10, 51–61.
Marsha, A., Sain, S.R., Heaton, M.J., Monaghan, A.J., Wilhelmi, O.V., 2016. Influences of climatic and population changes on heat-related mortality in Houston, Texas, USA. Climate Change. http://dx.doi.org/10.1007/s10584-016-1775-1.
Martin, S.L., Cakmak, S., Hebbern, C.A., Avramescu, M.-L., Tremblay, N., 2012. Climate change and future temperature-related mortality in 15 Canadian cities. Int. J. Biometeorol. 56, 05–619.
Martinez, G.S., Baccini, M., Ridder, K.D., Hooyberghs, H., Lefebvre, W., Kendrovski, V., Scott, K., Spasenovska, M., 2016. Projected heat-related mortality under climate change in the metropolitan area of Skopje. BMC Public Health 16, 407.
McMichael, A.J., Woodruff, R.E., Hales, S., 2006. Climate change and human health: present and future risks. Lancet 367 (9513), 859–869.
Murari, K.K., Ghosh, S., Patwardhan, A., Daly, E., Salvi, K., 2015. Intensification of future severe heat waves in India and their effect on heat stress and mortality. Reg. Environ. Chang. 15, 569–579.
O'Neill, B.C., Kriegler, E., Riahi, K., Ebi, K.L., Hallegatte, S., Carter, T.R., Mathur, R., van Vuuren, D.P., 2014. A new scenario framework for climate change research: the concept of shared socioeconomic pathways. Clim. Chang. 122, 387–400.
Patz, J.A., McGeehin, M.A., Bernard, S.M., Ebi, K.L., Epstein, P.R., Grambsch, A., Gubler, D.J., et al., 2000. The potential health impacts of climate variability and change for the United States: executive summary of the report of the health sector of the U.S. National Assessment. Environ. Health Perspect. 108 (4), 367–376.
Patz, J.A., Campbell-Lendrum, D., Holloway, T., Foley, J.A., 2005. Impact of regional climate change on human health. Nature 438 (7066).
Petkova, E.P., Horton, R.M., Bader, D.A., Kinney, P.L., 2013. Projected heat-related mortality in the U.S. urban northeast. Int. J. Environ. Res. Public Health 10, 6734–6747.
Petkova, E.P., Vink, J.K., Horton, R.M., Gasparrini, A., Bader, D.A., Francis, J.D., Kinney, P.L., 2017. Towards more comprehensive projections of urban heat-related mortality: estimates for New York City under multiple population, adaptation, and climate scenarios. Environ. Health Perspect. 125, 47–55.
Sarofim, M.C., Saha, S., Hawkins, M.D., Mills, D.M., Hess, J., Horton, R., Kinney, P., Schwartz, J., St. Juliana, A., 2016. Temperature-related Death and Illness. The Impacts of Climate Change on Human Health in the United States: A Scientific Assessment. U.S. Global Change Research Program, Washington, DC, pp. 43–68. http://dx.doi.org/10.7930/J0MG7MDX.
Schwartz, J.D., Lee, M., Kinney, P.L., Yang, S., Mills, D., Sarofim, M.C., Jones, R., Streeter, R., St. Juliana, A., Peers, J., Horton, R.M., 2015. Projections of temperature-attributable premature deaths in 209 U.S. cities using a cluster-based Poisson approach. Environ. Health 14 (85).
Stone, B., Vargo, J., Liu, P., Habeeb, D., DeLucia, A., Trail, M., Hu, Y., Russell, A., 2014. Avoided heat-related mortality through climate adaptation strategies in three US cities. PLoS One 9, e100852.
World Health Organization (WHO), 2014. Quantitative Risk Assessment of the Effects of Climate Change on Selected Causes of Death, 2030s and 2050s Prepared by Public Health & Environment Department, Health Security & Environment Cluster of World Health Organization.
Wu, J., Zhou, Y., Gao, Y., Fu, J.S., Johnson, B.A., 2014. Estimation and uncertainty analysis of impacts of future heat waves on mortality in the Eastern United States. Environ. Health Perspect. 122 (1), 10–16.